Remarks

Claims 1, 9-11, 21-22, 24, 26-29, 31-32, 35-40 are amended, claims 33-34 and 41-48 are canceled, and claims 49-52 are added. Claims 1-32, 35-40 and 49-52 are pending in this application.

The specification has been amended as requested by the Examiner to correct the informalities noted on page 2 of the Office Action.

The 35 U.S.C. § 112, First Paragraph, Rejections

A. The Examiner rejected claims 1-37 as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicant respectfully traverses this rejection. Applicants assert that the disclosure in the instant specification fully complies with the "written description" requirement of 35 U.S.C. § 112, first paragraph.

With respect to the written description requirement, the Examiner alleges that the specification, as originally filed, does not provide support for an antibody or other detection reagent having an IC_{50} for des-arginine fibrinopeptide B which differs from that for fibrinopeptide B "by less than 25%." Applicant respectfully submits that the amendments to the claims render the rejection moot.

The Examiner states that the specification provides sufficient characteristics for antibody populations or fragments thereof specific for the peptides. Applicant respectfully submits that the claims are limited to antiserum or an antibody or fragment thereof specific for peptides e.g., antiserum or an antibody or fragment thereof which recognizes Fibrinopeptide B (FPB) peptides and/or des-arginine Fibrinopeptide B (des-arginine FPB) peptides comprising amino acid sequence SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5 or SEQ ID NO:6.

The Examiner further alleges that adequate written description requires more than a mere statement that a product is part of the invention. . . . The product itself is required. (Office Action, page 5). It appears that the Examiner is equating an actual reduction to practice with adequate written description.

The high state of the art of antibody selection and the high state of knowledge regarding the structure of antibodies provides one of ordinary skill in the art with the sufficient background to fully understand and practice the present invention. The function of the written description requirement is to ensure that a patent is granted to inventors who had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by them; how the specification accomplishes this is not material. *In re Smith*, 178 U.S.P.Q. 620 (C.C.P.A. 1973). Therefore, the test for written description under 35 U.S.C. § 112, first paragraph, is whether the originally filed specification reasonably conveys to a person having ordinary skill in the art that Applicants had possession of the subject matter later claimed. M.P.E.P. § 2163.02. See also, *In re Kaslow*, 217 U.S.P.Q. 1089 (Fed. Cir. 1983). What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. M.P.E.P. § 2163.II.A.3(a) (citing to *Hybritech Inc. v. Monoclonal Antibodies, Inc.,* 802 F2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986)). An inventor is not required to describe every detail of the invention.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. M.P.E.P. § 2163.II.A.3(a)(ii). Thus, actual reduction to practice is only one of several ways in which Applicants can satisfy the Written Description requirement.

Furthermore, disclosure of an antigen fully characterized by its structure, formula, chemical name, physical properties, or deposit in a public depository provides an adequate written description of an antibody claimed by its binding affinity to that antigen. *Noelle v. Lederman*, 355 F.3d 1343, 1349, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004); MPEP § 2163. Applicant respectfully submits that the present specification describes and claims antibodies that

bind several antigens and provides clear guidance for production of antibodies through the use of these antigens, including a hybridoma cell line or a monoclonal antibody elicited by the antigen, e.g., Fibrinopeptide B antigen. Thus, the present application provides an adequate written description of the claimed invention and therefore meets the written description requirement under 35 U.S.C. § 112, first paragraph.

B. The Examiner rejected claims 7, 9-10, 27, 31, 33, 36 and 39 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. In particular, the Examiner alleges that the specification does not reasonably provide description of or enablement for any cell line producing a monoclonal antibody as instantly claimed. Applicant respectfully traverses this rejection. Applicants assert that the disclosure in the instant specification fully complies with the "written description" and "enablement" requirement of 35 U.S.C. § 112, first paragraph.

Applicant respectfully submits that producing antibodies in accordance with the present invention requires only antibody technology conventional in the art (see, e.g., Specification, page 16, lines 17-20). The specification of the present invention discloses how to construct and produce antibodies, provides means to identify monospecific antibodies, provides methodology to conjugate monospecific antibodies of the present invention to a detectable group, and discloses detailed methods of how to use the antibodies of present invention (see, e.g., Specification, pages 20-23). Furthermore, the instant claims are fully enabled when the specification is analyzed in view of the high state of the relevant art and the nature of the relevant art. M.P.E.P. § 2164.06(b) states:

> In *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), the court reversed the rejection for lack of enablement under 35 U.S.C. 112, first paragraph, concluding that undue experimentation would not be required to practice the invention. The nature of monoclonal antibody technology is such that

> experiments first involve the entire attempt to make monoclonal hybridomas to determine which ones secrete antibody with the desired characteristics. The court found that the specification provided considerable direction and guidance on how to practice the claimed invention and presented working examples, that all of the methods needed to practice the invention were well known, and that there was a high level of skill in the art at the time the application was filed. Furthermore, the applicant carried out the entire procedure for making a monoclonal antibody against HBsAg three times and each time was successful in producing at least one antibody which fell within the scope of the claims.

Thus, the present application provides an adequate written description of the claimed invention and is fully enabling and therefore meets requirements under 35 U.S.C. § 112, first paragraph. Therefore, Applicant respectfully requests that the rejection of the claims under 35 U.S.C. § 112, first paragraph, be withdrawn.

The 35 U.S.C. § 112, Second Paragraph, Rejection

The Examiner rejected claims 1-10, 21 and 35-40 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant respectfully traverses this rejection.

With regards to claims 1-10 and 35-40, Applicant has removed the phrase "defined by" from the claims. Applicant respectfully submits that the amendments to claims 1-10 and 35-40 render the rejection moot.

Claims 1-8, 9-10 and 35-37 were rejected for containing improper Markush language. Applicant respectfully submits that the amendments to the claims render these rejections moot.

Applicant thanks the Examiner for noting the dependency of claim 21. Applicant respectfully submits that Applicant has amended claim 21 in manner that renders the rejection moot

Applicant requests that the rejection of the claims under 35 U.S.C. § 112, second paragraph, be withdrawn.

The 35 USC §102 Rejections

The Examiner rejected claims 1-7, 9-15, 21-27, 35-36 and 38-39 as allegedly being anticipated under 35 U.S.C. § 102(e) by Kudryk *et al.* (U.S. Patent No. 5,876,947) and under 35 U.S.C. §102(a) by Kudryk *et al.* (WO 99/05176). These two Kudryk *et al.* references are identical in content. Therefore, the rejections are addressed collectively below.

Applicants respectfully traverse these rejections. The standard for anticipation is one of strict identity, and to anticipate a claim for a patent a single prior art source must contain all its elements. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 U.S.P.Q.2d 90 (Fed. Cir. 1986); *In re Dillon*, 16 U.S.P.Q.2d 1987 (Fed. Cir. 1990). Furthermore, there must be no difference between the claimed invention and the disclosure, as viewed by a person of ordinary skill in the art. *Scripps Clinic & Res. Found. v. Genentech, Inc.*, 18 U.S.P.Q.2d 1001 (Fed. Cir. 1991).

Kudryk et al. disclose a monoclonal antibody produced by a hybridoma cell line referred to as P10. The "P10" antibody is disclosed to specifically bind to fibrinogen, fibrinopeptide B, des-Arg fibrinopeptide B, N-DSK and related proteins (see, for example, page 5, lines 7-13; page 12, lines 17-19; Figures 1C, 2C and 4 of WO 99/05176). Kudryk et al. disclose that in a competitive ELISA, the P10 antibody was found to be "substantially more reactive with intact fibrinogen" than FPB or des-Arg FPB (page 31, lines 17-19 of WO 99/05176). Kudryk et al. further disclose that the clinical use of P10 is limited because of such strong cross-reactivity with fibrinogen (paragraph bridging pages 31-32 of WO 99/05176). Thus, Kudryk et al. do not disclose/anticipate the presently claimed antibodies.

As discussed above, Kudryk et al. disclose that P10 is very reactive to fibrinogen in a competitive ELISA. Figure 7 of Kudryk et al.(WO 99/05176) illustrates the dose-response reactivity data collected from the assay that have been linearized by means of logit transforms (page 31, lines 14-15 of WO 99/05176). In Figure 7 of Kudryk et al., the intercept of LOGIT = 0 represents the IC_{50} for the various antigens (i.e., fibrinogen (170kDa), Bβ 1-13 (des-arginine FPB) and Bβ 1-14 (FPB). According to Figure 7 of Kudryk et al., the IC_{50} of fibrinogen is about 1-2 pmol.ml (nM), the IC_{50} of FPB is about 100 nM, and the IC_{50} of des-arginine FPB is about 100 nM. Thus, Kudryk et al. disclose that the P10 antibody has a much stronger affinity for intact fibrinogen than for free FPB.

Contrary to the presently claimed invention, the Kudryk et al. antibody binds fibrinogen fifty- to one hundred-fold more strongly than it binds free FPB. Furthermore, this binding profile makes P10 clinically limited, because of the strong cross-reactivity with fibrinogen (which would likely lead to an erroneous result if any amount of fibrinogen were to remain in the clinical sample; see, for example the paragraph bridging pages 31-32 of Kudryk et al. (WO 99/05176)).

Thus, Kudryk et al. do not disclose/anticipate the presently claimed antibodies. Therefore, Applicant respectfully request that the 102(e)/102(b) rejections of the claims be withdrawn.

Claims 38 and 40 were rejected under 35 U.S.C. § 102(b) for anticipation by Qureshi et al. (Thromb. Haemostatis 42:1316, 1979) in light of Eckhardt et al. (J. Clin. Invest. 67:809, 1981), Bilezikian et al. (J. Clin. Invest. 56:438, 1975), and Wilner et al.(Biochemistry 18:5078, 1979). Applicant respectfully traverses this rejection.

The standard for anticipation is one of strict identity, and to anticipate a claim for a patent a single prior art source must contain all its elements. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 U.S.P.Q.2d 90 (Fed. Cir. 1986); *In re Dillon*, 16 U.S.P.Q.2d 1987 (Fed. Cir. 1990). Applicant respectfully submits that this rejection is inappropriate under 102 and respectfully requests that if the Examiner intends to maintain the rejection that the Examiner present it as a 103 rejection in a non-final Office Action.

The claims in question relate to kits for detecting or monitoring thrombotic or thromboembolic disease. The Examiner's statement that "Qureshi et al. predicted the clinical application of determinations of plasma fibrinopeptide B determinations by determination of the peptide in urine" reads more into Qureshi et al. than is actually disclosed. Qureshi *et al.* does not disclose any relationship between plasma and urine levels of fibrinopeptide B. In fact, Qureshi et al. disclose that FPB is unstable in urine and would therefore have been predicted to be a poor marker in urine. Therefore, Applicant respectfully submits that Qureshi et al. do not disclose the presently claimed kit. Thus, Applicant respectfully request that the 102(b) rejection of claims 38 and 40 be withdrawn.

The 35 USC §103 Rejections

The Examiner rejected claims 1-17 and 21-40 under 35 U.S.C. § 103(a) as being unpatentable over Kudryk et al. (US 5,878,947) or Kudryk et al. (WO 99/05176), in view of Eckhardt et al. (J. Clin. Invest. 67:809, 1981). Applicants respectfully traverse this rejection.

As discussed above, Kudryk et al. do not disclose or suggest the antiserum or antibody or fragment thereof as presently claimed. Eckhardt et al. do not do not compensate for the deficiencies of the primary reference. Thus, Applicant respectfully requests that the rejection of the claims under 35 U.S.C. § 103 be withdrawn.

Double Patenting

The Examiner rejected claims 1-14, 18-37 and 38-40 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 6,673,561, if necessary, in view of Kudryk et al. (US 5,876,947 or WO 99/05176). These rejections are respectfully traversed.

Applicants respectfully submits that the claims as amended are not obvious over claims 1-23 of U.S. Patent No. 6,673,561, alone or in view of Kudryk et al. Accordingly, it is respectfully requested the rejections for obviousness-type double patenting be withdrawn.

Conclusion

Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney, **Monique M. Perdok Shonka, at (612) 373-6905**, to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

TIMOTHY A. MORRIS

By his Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(612) 373-6900

Date 2-23-07

By _____
Warren D. Woessner
Reg. No. 30,440

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being filed using the USPTO's electronic filing system EFS-Web, and is addressed to: Mail Stop Amendment, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this 23 day of July 2007.

CANDIS BUENDING

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Name

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Signature